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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/536,822	10/18/2005	Mitsuharu Hirai	0666.2510000/TGD/AFK	6627

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EXAMINER	
BERTAGNA, ANGELA MARIE	
ART UNIT	PAPER NUMBER
1637	
MAIL DATE	DELIVERY MODE
06/10/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/536,822	HIRAI ET AL.	
	Examiner	Art Unit	
	ANGELA BERTAGNA	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 February 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-4 and 11-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-4 and 11-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/26/09; 5/20/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 26, 2009 has been entered.

Claims 2-4 and 11-13 are currently pending. In the response, Applicant amended claims 2-4 and 11, canceled claims 1 and 8-10, and added claims 12-13.

The following include new grounds of rejection necessitated by Applicant's amendments to the claims. Any previously made rejections or objections not reiterated below have been withdrawn as being obviated by the amendment.

Information Disclosure Statement

2. Applicant's submission of an Information Disclosure Statement on February 26, 2009 and May 20, 2009 is acknowledged. Signed copies are enclosed.

Specification

3. The preliminary amendment filed on May 27, 2005 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not

supported by the original disclosure is as follows: (1) the recitation "the filter part 34" in paragraph 59.

Applicant is required to cancel the new matter in the reply to this Office Action.

It is noted that preliminary amendments that were not present in a national stage application as of the international filing date are not part of the original disclosure (see MPEP 1893.01(b)). In this case, Applicant has not stated where the above amendments to the specification find support in the original disclosure. It is noted that MPEP 2163.07 states, "Where a U.S. application as originally filed was in a non-English language and an English translation thereof was subsequently submitted pursuant to 37 CFR 1.52(d), if there is an error in the English translation, applicant may rely on the disclosure of the originally filed non-English language U.S. application to support correction of an error in the English translation document."

Claim Rejections - 35 USC § 112, 2nd paragraph

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 12 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 12 is indefinite, because it recites the limitation "the electric field" in line 2 and in lines 3-4. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 2-4, 11, and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kreader et al. (EP 0 979 868 A2; cited previously) in view of Helenius et al. (Proceedings of the National Academy of Sciences, USA (1976) 74(2): 529-532; cited previously) and further in view of Muller et al. (Molecular and Cellular Biology (1996) 16(1): 442-456; newly cited).

The instant claims are drawn to methods for purifying and concentrating nucleic acids using electrophoresis and surfactants.

Kreader teaches a method for purifying nucleic acids using electrophoresis (see abstract).

Regarding claims 2-4, the method of Kreader comprises altering the electric charge of an impurity (*i.e.* a positively charged protein) present in a sample containing nucleic acids and

placing the sample in an electric field to separate the nucleic acid from the impurity, thereby concentrating and purifying the nucleic acid (see paragraphs 17-19 and 27-31). In the method of Kreader, upon lowering the pH of the sample using glycine hydrochloric acid, the positively charged protein impurity migrates in the opposite direction relative to the nucleic acid when the sample is placed in an electric field (see paragraphs 18, 21, and 31). In other words, by lowering the pH of the nucleic acid-containing sample, the electric charge of the positively charged protein impurity becomes more positive, and as a result, the positively charged protein impurity migrates further in a direction opposite to that of the nucleic acid during the electrophoresis step.

Kreader does not teach that the methods comprise adding a cationic surfactant and a nonionic surfactant to the sample.

Helenius analyzed the electrophoretic mobility of seventeen hydrophilic proteins and five amphiphilic proteins in the presence of: (1) the nonionic surfactant Triton X-100, (2) a mixture of a nonionic surfactant (Triton X-100) and an anionic surfactant (sodium deoxycholate), and (3) a mixture of a nonionic surfactant (Triton X-100) and a cationic surfactant (CTAB) (see abstract and page 529). Regarding claims 2-4, 11 and 13, Helenius teaches that the amphiphilic proteins migrated toward the anode in the presence of the Triton X-100/sodium deoxycholate mixture and toward the cathode in the presence of the Triton X-100/CTAB mixture (see abstract, pages 530-531, and Figures 2-4). Helenius teaches that the amphiphilic proteins interact with the mixtures of charged and nonionic surfactant molecules to form protein-surfactant complexes comprising neutral and charged surfactant molecules (page 529, column 1). Helenius states that "The net charges of the complexes are thus dependent on the charge of the detergents used, resulting in a clear-cut difference in electrophoretic mobility of the amphiphilic proteins when electrophoresed

in cationic and anionic detergent mixtures (page 529, column 1)." Helenius also states that "The detergent-induced shift in mobility provides a simple, rapid, and sensitive method for distinguishing between hydrophilic and amphiphilic proteins (abstract)."

Further regarding claims 3, 4, 11, and 13, Helenius expressly teaches that using a mixture of a nonionic and cationic surfactant is desirable to keep the structures of the protein-surfactant complexes as constant as possible (see page 531, column 1). Helenius also teaches that the cationic surfactant and nonionic surfactants compete to adsorb the different proteins subjected to electrophoresis (pages 529 and 531).

Muller teaches a method for analyzing plasma proteins by charge shift electrophoresis (page 444). In the method of Muller, charge shift electrophoresis as taught by Helenius was performed at an acidic pH, specifically pH 6.8 (page 444).

It would have been *prima facie* obvious for one of ordinary skill in the art at the time of invention to apply the teachings of Helenius to the method of Kreader. An ordinary artisan would have been motivated to further include a mixture of a nonionic and a cationic surfactant when practicing the method of Kreader in order to shift the migration of contaminating amphiphilic proteins present in the sample of Kreader to the cathode (*i.e.* in the opposite direction from the nucleic acids), since Helenius taught that detergent-induced mobility shifts provided a rapid, simple, and sensitive method for discriminating between differently charged species present in a sample (see abstract and page 531, column 2). An ordinary artisan would have recognized from the teachings of Helenius that adding a mixture of a nonionic and cationic surfactant to the mixture of Kreader would have achieved the same function as the pH reduction taught by Kreader, namely, electrophoretic migration of an impurity present in the sample in a

direction opposite to that of the nucleic acids, and therefore, would have been motivated to alter the electrophoretic migration of an impurity present in the sample of Kreader by using a mixture of non-ionic and cationic surfactant in combination with the low pH condition taught by Kreader. As noted in MPEP 2144.05, it is *prima facie* obvious to combine art-recognized equivalents known to be useful for the same purpose in the absence of unexpected results. Since Helenius taught that the net charge of the surfactant mixture determined the electric charge of the protein-surfactant complexes (see page 529, column 1), an ordinary artisan would have had a reasonable expectation of success in applying the teachings of Helenius to the method of Kreader. Also, since Muller taught that the charge shift electrophoresis method of Helenius could be conducted at an acidic pH (see page 444), an ordinary artisan would have had a reasonable expectation of success in using the mixtures of surfactants taught by Helenius at the low pH conditions of Kreader. Finally, regarding claims 4 and 13, an ordinary artisan would have recognized that the concentrations of the nonionic and cationic surfactants concentrations were results-effective variables that should be optimized in order to maximize the removal of protein contaminants without hindering nucleic acid separation. An ordinary artisan would have optimized these results-effective variables using routine experimentation and would have had a reasonable expectation of success in doing so. As noted in MPEP 2144.05, performing routine experimentation to optimize results-effective variables, such as concentration is *prima facie* obvious in the absence of unexpected results. Thus, the methods of claims 2-4, 11, and 13 are *prima facie* obvious over Kreader in view of Helenius and further in view of Muller in the absence of secondary considerations.

7. Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kreader et al. (EP 0 979 868 A2; cited previously) in view of Helenius et al. (Proceedings of the National Academy of Sciences, USA (1976) 74(2): 529-532; cited previously) and further in view of Muller et al. (Molecular and Cellular Biology (1996) 16(1): 442-456; newly cited) and further in view of Smolko et al. (US 6,284,117 B1; newly cited).

Claim 12 is drawn to the method of claim 2, wherein an electric field is applied to the sample for a first time period at a first voltage to remove excess ions from the sample, and then the electric field is applied to the sample for a second time period at a second voltage to concentrate and purify the nucleic acid.

The combined teachings of Kreader, Helenius, and Muller result in the methods of claims 2-4, 11, and 13, as discussed above.

The combined teachings of Kreader, Helenius, and Muller do not suggest conducting the electrophoresis step in the manner required by claim 12.

Smolko teaches a method of desalting low volume samples that comprises applying an electric field to rapidly and efficiently desalt the sample (see abstract, column 2, lines 27-47, and column 3, line 55 – column 4, line 5). Smolko states, "The high ionic strength level in a sample solution inhibits electronic transport of molecules that are sensitive to an electric field, such as nucleic acids. This is because as electronic potential is applied to the solution, if ions are present, they tend to carry charge and are transported instead of the larger molecules of interest (column 2, lines 58-63)."

It would have been *prima facie* obvious for one of ordinary skill in the art at the time of invention to apply the teachings of Smolko to the method resulting from the combined teachings

of Kreader, Helenius, and Muller. Specifically, an ordinary artisan would have been motivated to reduce the salt concentration in the nucleic acid samples of Kreader prior to conducting the electrophoresis method, since Smolko taught that high salt concentrations inhibited the electronic transport of molecules, such as nucleic acids (column 2, lines 58-63). An ordinary artisan would have been motivated to reduce the salt concentration using any method or device known in the art to be suitable for this purpose, such as the rapid and efficient method taught by Smolko, recognizing its suitability for the intended purpose. As noted in MPEP 2144.07, it is *prima facie* obvious to select a known material or method based on its suitability for the intended purpose in the absence of unexpected results. Thus, the method of claim 12 is *prima facie* obvious in view of the combined teachings of the cited references in the absence of secondary considerations.

Response to Arguments

8. Applicant's arguments filed on February 26, 2009 do not appear to explicitly address the objection to the specification. The amendment to the specification filed on February 26, 2009 addresses all of the previously made objections to the specification except for the requirement to delete the phrase "the filter part 34" in paragraph 59. As a result, the objection to the specification for incorporating new matter via the preliminary amendment filed on May 27, 2005 has been maintained.

Applicant's remaining arguments filed on February 26, 2009 have been considered, but they are moot in view of the new grounds of rejection presented above.

Conclusion

9. No claims are currently allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANGELA BERTAGNA whose telephone number is (571)272-8291. The examiner can normally be reached on M-F, 9- 5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kenneth R Horlick/
Primary Examiner, Art Unit 1637

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